Predicting COVID-19 Clinical Protective Immunity From SARS-CoV-2 T Cell Responses

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Amanda M. Buck[1], Darra Drucker[1], Michael J. Peluso[1], Steven G. Deeks[1], Rachel L. Rutishauser[1], Timothy J. Henrich[1], Amelia N. Deitchman[1]

[1]University of California San Francisco, San Francisco, CA, United States

BACKGROUND

- SARS-CoV-2 produces variable immune responses leading to different levels of immune protection.
- Links between neutralizing antibody level (NAb) and protective immunity has been well characterized after infection and vaccination. [2]
- Specific T cell responses tend to be more variable.
  - Have broad implications on long-term immunity.
  - Their role in protective immunity has not been as clearly defined.
- Using data from our prospective cohort study [1] and studies of clinical protective immunity (from vaccines) [2], we predicted protective immunity over time in relation to SARS-CoV-2-specific T cell dynamics.

METHODS

- Samples were collected from volunteers in the UCSF Long-term Impact of Infection with Novel Coronavirus (LIINC) COVID-19 recovery study. All participants had a history of SARS-CoV-2 infection confirmed with nucleic acid amplification testing. (n=70, 48% female)
- Simulated the Spike (S)-specific interferon-γ (IFNγ)+ CD4+, S-specific IFNγ+ CD8+, and nucleocapsid (N)-specific IFNγ+ CD4+ T cells over time from our published COVID-19 immune data [1].
  - Used previously developed linear mixed-effects models [1] to simulate 25%, 50%, 75%, and 100% T cell responses (n=500 patients).
  - Predicted NAbs from linear regression models developed from same cohort of NAb levels versus T cell responses.
- Protective immunity from NAb titers was then predicted from a published model [2].

- Separately, we used the above models to simulate T cell response after COVID-19 vaccination.

Certain T cell responses can reliably predict protective immunity and may be *intrinsically* linked.

Figure 1. The relationship between neutralizing antibodies (NAbs) and nucleocapsid (N)-specific IFNγ+ CD4+ T cells enabled the prediction of protective immunity over time.

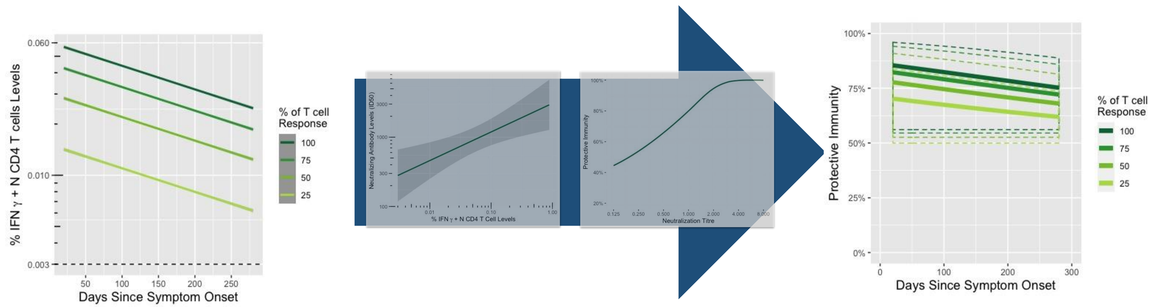
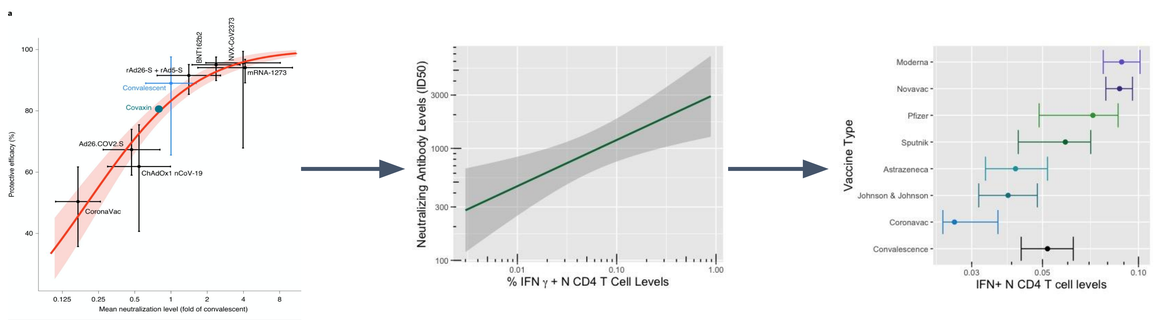


Figure 2. IFNγ+ N CD4+ T cell levels were predicted from NAb levels induced by vaccination.



Khoury, et al. Nature Medicine 2021

RESULTS

- Virus-specific T cell responses resulted in similar protective immunity across T cell subsets despite wide variation over time.
  - 55-98% IFNγ+ S CD8
  - 51-99% IFNγ+ S CD4
  - 56-98% IFNγ+ N CD4
- With a 75% reduction in T cell immunity, protective immunity overall did not drop more than 7% in response.

- Predicted T cell response from NAb levels varied widely across vaccines (range 0.013% - 0.180%).

CONCLUSIONS

- For SARS-CoV-2, certain T cells responses can reliably predict protective immunity and may be intrinsically linked.
- Simulating dampened T cell response to mimic a more virulent strain or inadequate immune response, demonstrated that dampened T cell response may not be responsible for inadequate protective immunity in these scenarios.
- While there are other subsets of T cells that do not have a clear relationship, the ones that do should be present in immune response discussion along side of NAbs.
  - Separate studies need to be done to elucidate the role of T cells in contributing to protective immunity.
- In the absence of prospective clinical data, similar models may be utilized to explore the impact of potential therapeutics on immune responses and resulting protective immunity.

- As new variants emerge and more booster vaccinations are required, protective immunity should also be analyzed in regard to various lymphocyte subsets.

ADDITIONAL KEY INFORMATION

References

[1] Peluso, et al.Cell Reports 2021.

[2] Khoury, et al. Nature Medicine 2021.

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Contact Information

Amanda M. Buck, BS

Graduate Researcher

University of California, San Francisco

Amanda.Buck@ucsf.edu